DETAILED ACTION

The response filed **3/3/08** presents remarks and arguments to the office action mailed **10/3/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Status of Claims

Claims 1-9 and 28-32 are cancelled. Claims 10, 16, 24 and 33 are currently amended.

Claims 10-27 and 33-34 are pending.

Allowable Subject Matter over prior art (claims 16-27)

The US patents 6,369,261, 6313107 and 6,313,107 are cited to show the state of the art. Set compound teaches core structures of formulae in instant claims 16-27, however, do not teach the substituent of Y as an alkyne. The set compound is devoid of the Y group that is required of claims 16-27. Thus the prior art does not anticipate nor suggest instant claims 16-27. A recently allowed patent has the claimed compound where Y is an alkyne, See patent US 7,351,737.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Vasudevan et al., US 6,313,107.

Vasudevan et al. teach the compounds of a cytochrome P450 retinoic acid inducible (CYP450RAI) enzyme can also be used in co-administration with retinoids See abstract. With respect to the compound, see col. 27, lines 20-29 for the generic structure and specifically compound 8, wherein X_1 in the art is defined as methyl cyclopropyl-N and R_2 is H as required by the instantly claimed compound (I) as in claimed 10-14. . As defined by Moss, INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY and INTERNATIONAL UNION OF BIOCHEMISTRY AND MOLECULAR BIOLOGY IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN), the term Vitamin A should be used as the generic descriptor for retinoids exhibiting qualitatively the biological activity of retinol. Thus claims 10-14 (inpart) and claim 15 are anticipated.

Maintained Claim Rejections - 35 USC § 103

Claims **10-15 are** rejected under 35 U.S.C. 103(a) as being obvious over Johnson et al., US 6369,261 and Van Scott et al. US 3,932, 665 (as evident by).

Applicant argues that Claims 10-15 are drawn to methods using compounds in co-administration with Vitamin A and retinoic acid which compounds are neither disclosed nor structurally suggested by these two references. Therefore, these claims are not obvious over the cited references. In the event the Examiner maintains the view that the

compounds defined in independent Claim 10 are structurally obvious over either of the two cited references, the applicant respectfully request the Examiner to specifically point out the structure or structures in the reference(s) that would, in the Examiner's view, render the compound(s) obvious to be used in the claimed method.

In response, the compound of claim 10 is disclosed at col. 22, lines 55-65 as compound 12, wherein the $X_{1\text{ in the art is defined as methyl cyclopropyl-N}}$ and R_2 is H as required by the instantly claimed compound (I), see col. 23, lines 1-10, Table 5 wherein the compound is identified as compound 8. At col. 17, lines 49-52 the patent discloses the CP450RAI may be co-administered with formulations containing retinoids.

Careful consideration has been given, however, the argument is found not persuasive. The rejection is maintained below.

Johnson et al. reference teaches co-administration of compound of formula I with compounds of retinoic acid; see col. 17, lines 49-52. (vitamin A as evident by Van Scott et al. col. 2, lines 29-31), wherein the compound of formula I is specific inhibitor of cytochrome P450RAI (see col. 1, lines 6-10) is used (see col. 29, lines 25-43) as required by instant claims 10-15 for the treatment of psoriasis (see col. 1, lines 30-31). The substituents of the instant claims are also taught, R_1 and R_2 are hydrogen's and R_3 is CH_3, (see formula col. 29, lines 25-43).

One of ordinary skill in the art would have been motivated to use the teachings of Johnson et al. by administering the compound of claim 10 where in the compound has a cytochrome P450RAI activity with a retinoic acid for the treatment of psoriasis because as taught by Johnson et al. that administering certain inhibitors with cytochrome P450RAI results in significant increase in endogenous retinoic acid levels. The combination with retinoic acid as the reference teaches these compounds can be used

with retinoic acid (see col. 10, lines 53) because retinoic acids are useful in the treatment of skin related disease.

Thus, the claimed invention was prima facie obvious to make and use at the time it was made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al., US 6369,261 or Vasudevan et al., US 6,313,107 in view of Granger et al., US 20040043044

Johnson et al. reference teaches co-administration of compound of formula I with compounds of retinoic acid, see col. 17, lines 49-52 or Vasudevan et al. as supra.

Wherein the X_1 in the art is defined as methyl cyclopropyl-N and R_2 is H as required by the instantly claimed compound (I), see col. 23, lines 1-10, Table 5 wherein the compound is identified as compound 8. Also see col. 17 of Johnson et al. lines 23-26 discloses treatment of dermotoses will be effected by administering one or more compounds of the invention.

The reference however fails to teach the pharmaceutical composition comprises compound of both formulae I and II.

Granger et al. teach that natural and synthetic vitamin A (retinol) compounds have been used extensively to "treat a variety of skin disorders, e.g., acne, wrinkles, psoriasis, age spots, and discoloration." The reference also teaches that certain compounds, termed "boosters," when used alone or in combination with each other, potentiate the action of retinoids by increasing the conversion of the retinoids to retinoic acid. One of the "boosters" cited by Granger are inhibitors of cytochrome P450 dependent retinoic acid oxidation ([0006]). The reference teaches compositions include a retinoid (e.g. retinol, retinyl esters, retinal, retinoic acid) co-present with a booster or

combination of boosters to optimize efficacy of the composition. (See page 1 [0001-0007, O115]).

Therefore one of ordinary skill in the art would have been motivated to add cytochrome P450 inhibitors as boosters of different structures to boost the treatment of skin disease. Therefore, one would be motivated to formulate a pharmaceutical topical composition for the treatment of skin disease such as psoriasis. Also see col. 17 of Johnson et al. lines 23-26 discloses treatment of dermatoses will be effected by administering one or more compounds of the invention, therefore having one or more compounds that are characterized as CP450RAI will be expected to boost the treatment as disclosed by Granger et al.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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6/17/08